Total Photolytic Synthesis of (±)-Pronuciferine, (±)-*O*-Methylorientalinone, and (±)-*O*-Methylkreysiginone

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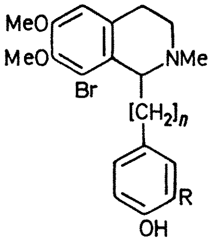
Summary Photolysis of 8-bromo-1,2,3,4-tetrahydro-1-(4-hydroxybenzyl)-6,7-dimethoxy-2-methylisoquinoline (**1**) gave (±)-pronuciferine (**4**); the same reaction of the phenolic bromoisoquinolines, (**2**) and (**3**), afforded (±)-*O*-methylorientalinone, (**5a**) or (**5b**), (±)-*O*-methylisoorientalinone, (**5b**) or (**5a**), and (±)-*O*-methylkreysiginone (**6a**).

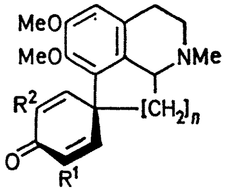
PREVIOUSLY, we reported the synthesis of the proaporphines[1] and homoproaporphines[2] by phenolic oxidative coupling from the corresponding diphenolic isoquinolines. However, without exception, this coupling reaction proceeds at the *ortho*- or *para*-position to the phenolic hydroxy-group. Therefore, we have been searching for a simple and general photocatalysed nucleophilic aromatic substitution or related reaction,[3] and herein report the synthesis of the proaporphines and homoproaporphines by photolysis of phenolic bromoisoquinolines.

The bromoisoquinoline (**1**) was irradiated in stirred aqueous methanol in the presence of sodium hydroxide at room temperature. The irradiation (Hanovia 450 W mercury lamp, Pyrex filter) yielded (±)-pronuciferine (**4**) (10%), an alkaloid from Papaver species,[4] identical with the authentic sample.[1] When the photolysis was performed in ethanolic sodium hydroxide solution in the presence of copper powder, the yield increased to 17%. The same reaction of the phenolic bromoisoquinoline (**2**) gave a mixture of *O*-methylorientalinone and *O*-methyliso-orientalinone (**5a**) and (**5b**)[5] that differed in configuration at the spiro-centre.[6] These were separated by fractional recrystallisation of the picrate. The physical and spectroscopic data of both compounds are identical with those published.[7]

Photolysis of the phenolic bromophenethylisoquinoline (**3**) gave an inseparable mixture of *O*-methylkreysiginone (**6a**) and its spiro-isomer (**6b**)[8] in 1 : 1 ratio (n.m.r. spectrum[8]).



(**1**) R = H, $n = 1$
(**2**) R = OMe, $n = 1$
(**3**) R = OMe, $n = 2$



(**4**) $R^1 = R^2 = H, n = 1$
(**5a**) $R^1 = OMe, R^2 = H, n = 1$
(**5b**) $R^1 = H, R^2 = OMe, n = 1$
(**6a**) $R^1 = OMe, R^2 = H, n = 2$
(**6b**) $R^1 = H, R^2 = OMe, n = 2$

It may be concluded that photolysis of phenolic 8-bromoisoquinolines under alkaline conditions is a useful method for synthesising the proaporphines and homoproaporphines.

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[1] T. Kametani and H. Yagi, *Chem. Comm.*, 1967, 366.

[2] T. Kametani, K. Fukumoto, H. Yagi, and F. Satoh, *Chem. Comm.*, 1967, 878; T. Kametani, F. Satoh, H. Yagi, and K. Fukumoto, *J. Org. Chem.*, 1968, **33**, 690.

[3] E. Havinga, R. D. deJongh, and M. E. Kronenberg, *Helv. Chim. Acta*, 1967, **50**, 2550; N. Kharasch, J. G. Alston, H. B. Lewis, and W. Wolf, *Chem. Comm.*, 1965, 242; W. Wolf and N. Kharasch, *J. Org. Chem.*, 1965, **30**, 2495; S. M. Kupchan and H. C. Wormser, *J. Org. Chem.*, 1965, **30**, 3935; S. M. Kupchan and H. C. Wormser, *Tetrahedron Letters*, 1965, 359.

[4] L. Kuhn and S. Pfeifer, *Pharmazie*, 1965, **20**, 520.

[5] A. R. Battersby, T. J. Brockson, and R. Ramage, *Chem. Comm.*, 1969, 464.

[6] A. R. Battersby, T. H. Brown, and J. H. Clements, *J. Chem. Soc.*, 1965, 4550.

[7] S. Ishiwata and K. Itakura, *Chem. Pharm. Bull.* (*Tokyo*), 1970, **18**, 1224.

[8] T. Kametani, F. Satoh, H. Yagi, and K. Fukumoto, *J. Chem. Soc.* (*C*), 1970, 382.

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